

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/007375

International filing date (day/month/year)
06.07.2004

Priority date (day/month/year)
11.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/37, A61K35/78, A61K31/70, A61K31/7048, A61K8/97, A61Q19/06, A61P17/00

Applicant
INDENA S.P.A.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/007375

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/007375

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-11
	No: Claims	-
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-11
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	-

2. Citations and explanations

see separate sheet

Re Item V

Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.

- D1: PHLEBOLOGIE, vol. 23, no. 3, 1994, pages 71-77, XP009039687
- D2: ROSSI A B R ET AL: "CELLULITE: A REVIEW" J EADV. JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 14, no. 4, 2000, pages 251-262, XP009011440 ISSN: 0926-9959
- D3: BOMBARDELLI F ET AL: "AESCULUS HIPPOCASTANUM L" FITOTERAPIA, IDB HOLDING, MILAN, IT, vol. 67, no. 6, 1996, pages 483-511, XP000917088 ISSN: 0367-326X
- D4: WO 01/78674 A (CETERIS HOLDING B V AMSTERDAM ; BERARDESCA ENZO (IT)) 25 October 2001 (2001-10-25)
- D5: FR-A-2 740 681 (FABRE PIERRE DERMO COSMETIQUE) 9 May 1997 (1997-05-09)
- D6: EP-A-0 692 250 (INDENA SPA) 17 January 1996 (1996-01-17)
- D7: EP-A-0 680 761 (INDENA SPA) 8 November 1995 (1995-11-08)
- D8: EP-A-0 418 806 (INDENA SPA) 27 March 1991 (1991-03-27)

1. Novelty

None of the documents D1-D8 discloses the compositions as claimed. Claims 1-11 are therefore considered novel (Art. 33(2) PCT).

2. Inventive step

The problem underlying the present application was the provision of pharmaceutical compositions for treating panniculopathy (cellulite) and problems connected with venous insufficiency of the lower limbs.

The solution, according to the applicant was the provision of compositions as claimed.

The compounds or extracts visnadin, esculoside, *Ginkgo biloba* dimeric flavones, amentoflavone, escin, escin beta-sitosterol, sericoside and *Centella asiatica* extract

are already known in the art for treating cellulite or venous insufficiency.

D1: *Centella asiatica*, esculoside, escin and *Ginkgo biloba* for treating venous insufficiency (CVI).

D2: *Ginkgo biloba* and *Centella asiatica* for treating cellulite and to increase venous blood flow.

D3: Escin and escin beta-sitosterol for treating cellulite.

D4: *Centella asiatica* extracts for treating wrinkles-like cellulite. A preferred embodiment is the combination of *Centella* extracts with amentoflavone.

D5: *Viburnum* extracts containing as active principle amentoflavone for treating cellulite.

D6: Esculoside and *Ginkgo biloba* or amentoflavone for treating cellulite.

D7: *Ginkgo biloba* and visnadine as cicatrizing agents for treating disorders due to venous insufficiency.

D8: Visnadine for the treatment of cellulitis and local perfusion deficiencies of the lower limbs.

The combination of known compounds for the same treatment can only be regarded as being inventive if a surprising/unexpected effect can be shown. However, the applicant has failed to proof such effect.

For this reason, no inventive step can be recognized from the application (Art. 33 (3) PCT).